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Primer

Mapping vertebrate embryos

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A major challenge in embryology is to understand how cells become specialized into distinct lineages and assembled into a pattern of tissues that will make up the embryo. The discovery that patterns of gene expression are conserved among embryos of the favourite vertebrate species for laboratory study — zebrafish, frog *(Xenopus)*, chick and mouse — has led to a surge of interest in finding out how similar development is in these embryos. This primer describes the organization of the body plan in the embryos of these four species. We will look at their 'fate maps', which are drawn by tracing the tissues that develop from particular regions of the early embryo and so can be used to predict the normal developmental fate of cells.

Setting up the germ layers

Immediately after fertilization, development of the vertebrate embryo is preoccupied with building up cell numbers. An important milestone is reached when cell numbers are sufficient to allow gastrulation, the process of establishing a body plan, when distinct cell layers, called the germ layers, first form. These layers are the ectoderm (outer), mesoderm (middle) and endoderm (inner), which go on to make distinct tissues in the embryo. Broadly speaking, ectoderm makes skin and nervous tissue, mesoderm the muscles, bones and vasculature, and endoderm the gut.

Vertebrate embryos arrive at gastrulation at different sizes and shapes, and their regions have, for historical reasons, confusingly different names (Fig. 1a). In fish and frog embryos, the 'animal' (upper) hemisphere and the equatorial 'marginal' zone coincide, respectively, with future ectodermal and mesodermal tissues. Endoderm arises from the vegetal (lower) half of the frog embryo, but prospective endoderm in the fish is confined to the edges of the curved, disc-shaped embryo (known as the blastoderm). Like the fish embryo, the early chick embryo is made up of a blastoderm, a flattened disc of cells on top of a ball of yolk; in the mouse, by contrast, the cells that will become the embryo proper are called the epiblast, and this is surrounded by cells that will not contribute to the embryo (Fig. 1a). No obvious animal–vegetal subdivision is found in chick and mouse embryos, but the cells at the outer edge of each contain progenitors of the extraembryonic membranes that provide the embryo with nutrition and blood cells.

If we imagine that this domain of extraembryonic tissues is equivalent to the vegetal part of a frog or fish embryo, the centre of the chick blastoderm and the distal end of the mouse epiblast (furthest from the site of implantation) might correspond to the animal hemispheres of the fish and frog embryos (Fig. 1a). From this perspective, ectodermal progenitors in chick and mouse embryos occupy an 'animal pole' position, as in the frog and fish, while the mesodermal progenitors are found to the sides, adjoining the 'vegetal' tissues, again as in the frog and fish. The endodermal progenitors in the chick and mouse, however, are in totally different positions along this 'animal–vegetal' axis. Other variations of the theme are also evident: there are obvious discrepancies in the relative proportion of tissues allocated to various lineages, and the overlap of tissue domains also varies among the four species (Fig. 1b).

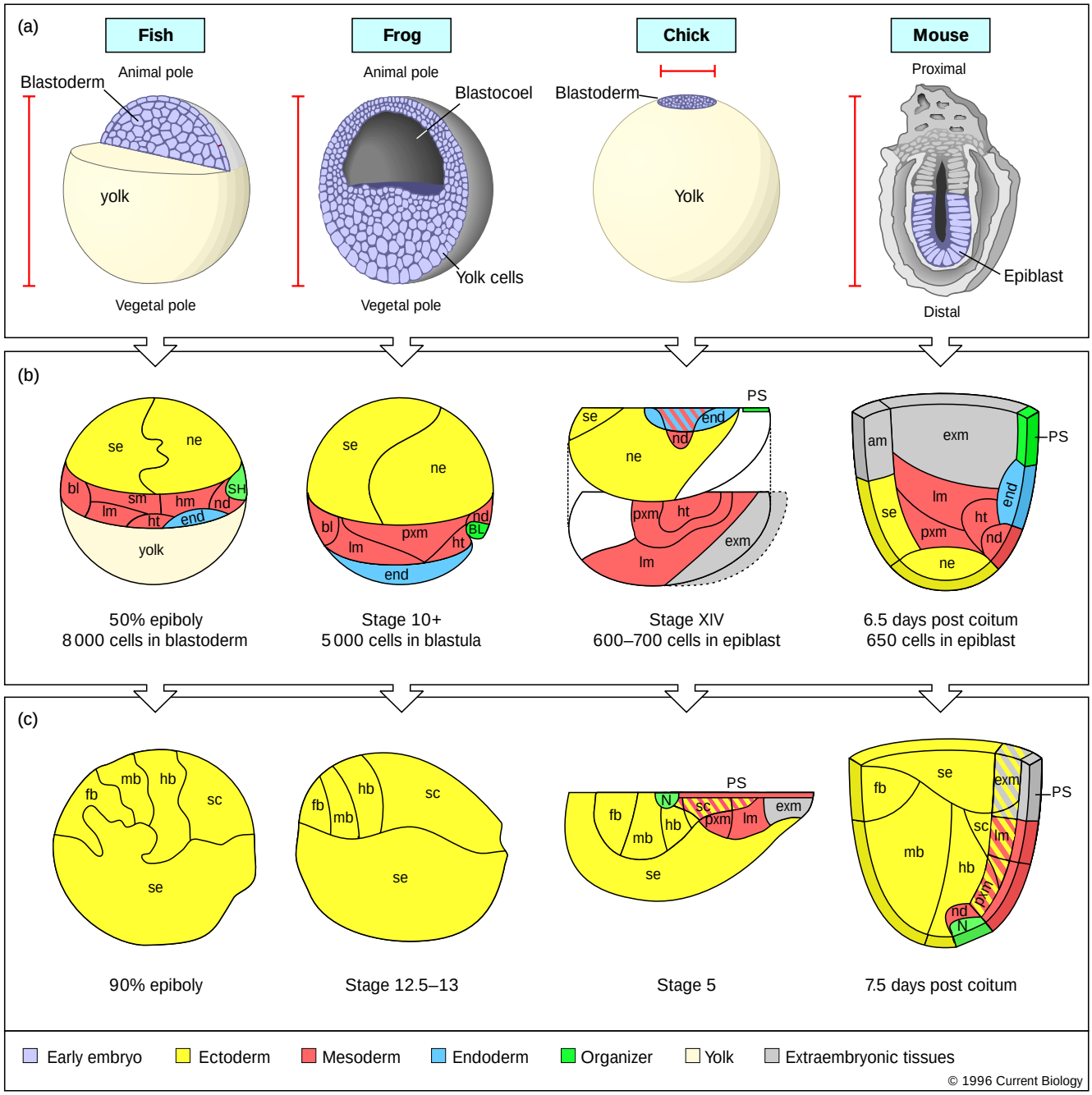
Focussing on the organizer

In each of the four embryos, a special group of cells can be identified as the organizer, which is able to induce the formation of a whole new body axis if transplanted to a new site in the embryo; the cells also express similar genes in each species (Fig. 2b). A striking homology between fate maps becomes evident when examining the arrangement of tissue progenitors relative to the organizer. In each case, progenitors of the mesoderm found on the dorsal (back) side of the embryo are closer to the organizer, with the ventral (belly) mesoderm and the blood-forming extraembryonic mesoderm furthest away. In fish, frog and mouse embryos, expression of the *Bmp4* and *even-skipped* genes marks some mesoderm as 'ventral', whereas cells associated with the organizer express genes characteristic of 'dorsal' mesoderm (Fig. 2). For the ectoderm, the progenitors of the central nervous system are next to the organizer and the surface (skin) ectoderm is further away. Moreover, finer mapping in the fish and mouse embryos reveals a head-to-tail pattern in the neural progenitors, with the organizer always abutting the tail-most (caudal) prospective neural tissues.

Converting one dimension into three

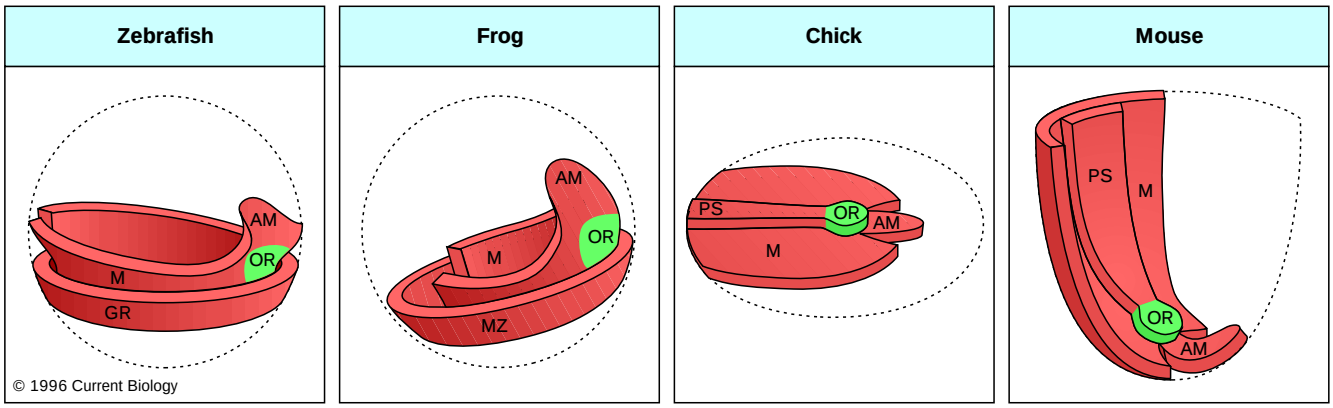
Gastrulation is accomplished by different cell movements in the four embryos (Fig. 1). The strategy varies from inward migration of individual cells at all points along the circumference of the fish embryo, through in-turning of a cohesive tissue sheet through a hole (the blastopore) in the frog, to cells sinking inwards along the primitive streak in chick and mouse. Whatever the mechanism, the single-layer embryo is transformed into three layers. Not only are the dorsal–ventral and anterior–posterior relationships of different tissue types maintained during this process, but the tissue components destined for specific body segments are also brought together (Fig. 1); variations in gastrulation confer species-specific

Figure 1



Fate maps for embryos of four vertebrate species, drawn with their normal topography (see text for further details). **(a)** Appearance of each embryo before gastrulation. Scale bars: fish, 500–600 μm; frog 1–2 mm; chick, 2-3 mm; mouse, 700 μm. **(b)** Fate maps at early gastrulation, drawn in normal topography. Embryos are aligned so that the 'organizer' is on the right hand side of each fate map. The organizer is found in the 'embryonic shield' (SH) of the zebrafish and the 'dorsal blastopore lip' (BL) of the frog embryo; the precursor of the organizer (the node) is first found as an integral part of the early primitive streak (PS), the first morphological landmark of the chick or mouse embryo. In representing the chick embryo, separate images of a blastoderm are shown to indicate germ layer precursors with overlapping distributions. **(c)** Fate maps for the ectodermal layers at the end of gastrulation (mesodermal and endodermal layers are not shown due to space constraints). The anterior–posterior axes are aligned horizontally in the figure, such that the the site of cell movement to the interior is on the posterior (right hand side) of the map. By this stage, the organizer is morphologically distinguishable at the anterior extremity of the primitive streak (N), as the Hensen's node (chick) or the node (mouse). Ectodermal tissues: ne, neuroectoderm, fb, forebrain; mb, midbrain; hb, hindbrain; sc, spinal cord; se, surface ectoderm. Mesodermal tissues: pxm, paraxial mesoderm; hm, head mesoderm; sm, somites; lm, lateral mesoderm; nd, notochord; ht, heart; bl, blood. Endodermal tissues: end, gut endoderm. Extraembryonic tissues: am, amnion ectoderm; exm, extraembryonic mesoderm.

Figure 2



(b)

	Germ ring / Marginal zone: Ventral, Primitive streak, Posterior				Germ ring / Marginal zone: Dorsal, Primitive streak, Anterior						Axial Mesoderm, Posterior				Axial Mesoderm, Anterior	
Gene families:	*Evx*	*Bmp*	*T*	Others	*T*	*Gsc*	*Forkhead*	*nodal*	*Lim*	Others	*T & Shh*	*Forkhead*	*Not*	Others	*Gsc*	*Lim*
Zebrafish	*eve1*		*ntl*		*ntl*	*gsc*	*axial, zf-FKH1*		*zflim*	*Shh*	*ntl*	*axial, zf-FKH1*	*flh*			*zflim*
Xenopus		*Bmp4*	*Xbra*	*Xnr-2*	*Xbra*	*gsc*	*Pintallavis*	*Xnr-3* *Xnr-1*	*Xlim-1*	*chordin* *noggin, Xnot2*	*Xbra*	*Pintallavis*	*Xnot*	*chordin* *noggin*	*gsc*	*Xlim-1*
Chick			*Ch-T*	*Hnf3β** *cNR1**	*Ch-T*	*gsc*	*Hnf3β*			*Cnot, cAct-RIIb* *cAct-RIIa*, Shh**	*Ch-T* *Shh*		*Cnot*		*gsc*	
Mouse	*Evx1*	*Bmp4*	*T*	*follistatin, Lim1*	*T*	*Gsc*	*Hnf3β*	*nodal*		*Shh*	*T, Shh*	*Hnf3β*				*Lim1*

(a) Topographical organization in gastrulating embryos of organizer (OR), axial mesoderm (AM; the central mesoderm made up of the chordamesoderm, head process and supportive notochord), newly formed mesoderm (M) and cells in the germ ring (GR) of the fish, marginal zone (MZ) of the frog, or primitive streak (PS) of chick and mouse. The axial mesoderm is depicted as an extension in the midline of the embryo of tissues from the node, towards the anterior (head) end of the embryonic body and underneath the neuroectoderm. Colours are as in Fig. 1. (b) The table summarizes the types of genes expressed in mesodermal precursors, organizer and axial mesoderm of the four vertebrate gastrula-stage embryos. These genes encode putative transcription factors, signalling molecules and receptors. In each column except the Organizer one, genes that are expressed more dorsally (fish and frog) or anteriorly (chick and mouse) are listed towards the right of the table. In the chick, genes that display asymmetrical (handed) expression in the primitive streak and Hensen's node are indicated by asterisks.

morphology but do not alter the blueprint.

In summary, fate maps are sufficiently consistent among vertebrate embryos for us to believe that some conserved mechanism of body patterning may operate during embryogenesis. Data on the fate maps are far from complete, however. Findings have often been interpreted from the perspective of the frog embryo, so some important differences might have been overlooked. Nevertheless, fate maps are particularly useful in interpreting the outcome of embryological experiments involving the gain or loss of gene functions and for assessing the relative importance of a cell's potency, lineage and movement in determining its fate.

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